

Remarks

Claims 1-20 are pending in the subject application. Favorable consideration of the pending claims is respectfully requested.

Applicants and Applicants' undersigned representative wish to express their sincere appreciation to Examiner Woolwine for the courtesy of the telephonic interview conducted with the undersigned on November 12, 2008, regarding the status of the current Office Action. Examiner Woolwine indicated that he will enter and give consideration to the Declaration under 37 CFR §1.132 of Dr. Peter Richardson and issue another Office Action (and if new grounds of rejection are made, the Action will be non-final). The remarks and amendments set forth herein are consistent with the substance of the interview and the Interview Summary and are believed to address the issue as discussed during the interview.

Claims 1-6 and 8-20 are rejected under 35 USC §103(a) as obvious over Richardson *et al.* (WO 01/06004) in view of Gu *et al.* (U.S. Published Application No. 2003/0180737). In addition, claim 7 remains rejected under 35 USC §103(a) as obvious over Richardson *et al.* (WO 01/06004) in view of Gu *et al.* (U.S. Patent Application No. 2003/0180737) and further in view of Fend *et al.* (1999). The Examiner asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to carry out first and second strand cDNA synthesis using the "single-pot" method of the Gu *et al.* publication when practicing the method of the Richardson *et al.* publication. Applicants respectfully traverse these grounds of rejection.

Applicants respectfully assert that the cited references, whether taken alone or in combination, do not teach or suggest the claimed invention. The Examiner asserts that it would have been obvious to adapt the method of the Richardson *et al.* publication so that the reverse transcription and amplification are carried out using the "single-pot" method of Gu *et al.* Applicants respectfully maintain that for their claimed invention, in order to establish a *prima facie* case of obviousness, it is necessary for the Patent Office to show that the ordinarily skilled artisan would have had some suggestion or motivation to combine the cited references. *In re Geiger*, 2 USPQ2d 1276 (Fed. Cir. 1987). In the instant Office Action, the Examiner disagrees that a suggestion or motivation to combine the cited references is required in the instant case, but asserts that the issue is

moot since the Examiner believes that motivation has been set forth in the rejection. Applicants respectfully maintain that a suggestion or motivation is required, even under *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) and further maintains that the Examiner has not established that the cited references provide the requisite motivation to combine the teachings of the Richardson *et al.* and Gu *et al.* publications. The Examiner previously asserted that combining two steps from the teachings in the art into a single step would have been obvious and that a suggestion that the ordinarily skilled artisan would not have recognized the advantage of doing so assumes that the artisan would have “lacked common sense.” Applicants respectfully maintain that the ordinarily skilled artisan would not have been able to predict the outcome of combining multiple chemical reaction steps into a single step. The ordinarily skilled artisan would not have looked to combine the teachings of the Richardson *et al.* and Gu *et al.* publications as there was no teaching or suggestion in the art that such a combination would yield desirable results, or that methods resulting from the combination would even work at all. It is only the subject application that teaches the desirability and operability of the claimed method. Applicants again note that hindsight reconstruction of the prior art to arrive at Applicant’s invention is not permissible. *In re Sponnoble*, 160 USPQ 237, 243 (CCPA 1969). In hindsight (viewed from having considered the teachings in Applicants’ specification), the fact that Applicants’ method works and possesses surprising advantages over the teachings in the art might have been “expected.” However, as noted above, hindsight reconstruction is expressly forbidden in making an obviousness determination. Without the benefit of hindsight, the ordinarily skilled artisan would not have combined the teachings of the cited references, and would not have expected the operability or surprising advantages possessed by Applicants’ claimed method.

Also under these rejections, the Examiner asserts that no data has been provided to establish that the claimed method is more efficient than the methods in the cited references. However, under the authority of *In re Marzocchi*, 169 USPQ 367 (CCPA 1971), Applicants’ statements concerning the claimed invention must be taken as true unless the Patent Office can recite specific reasons to doubt the validity of those statements. The Examiner has not provided evidence or teachings to doubt the validity of Applicants’ statements concerning the invention. Moreover, Applicants have submitted evidence herewith in the form of a Declaration from Dr. Peter Richardson, co-inventor on the cited Richardson *et al.* publication, that the method of the claimed invention possesses

unexpected and non-obvious advantages (e.g., increased reverse transcription efficiency) over the method taught in the cited publications.

Applicants respectfully assert that neither the cited references nor the Examiner provide any evidence that the results obtained with Applicants' claimed invention were predictable from the cited publications or from the general knowledge of a person of ordinary skill in the art. The U.S. Supreme Court has indicated that a combination of elements is unlikely to be deemed obvious when the combined elements yield unpredictable or unexpected results. *KSR International Co. v. Teleflex Inc.*, *supra*. Applicants respectfully maintain that there are unexpected advantages and unpredictable results associated with Applicants' claimed invention that are not suggested in, or that could not have been predicted from, the cited publications or the general knowledge of the ordinary artisan. Submitted with this Response is a Declaration under 37 CFR §1.132 by Dr. Peter Richardson. It is relevant to note that Dr. Richardson is the first named co-inventor on the Richardson *et al.* publication cited under these rejections. Thus, Dr. Richardson is very familiar with the teachings of the Richardson *et al.* publication and his comments should be given due weight. Applicants respectfully request that the Examiner consider and make of record Dr. Richardson's Declaration in the subject application.

As indicated in the Declaration under 37 CFR §1.132 by Dr. Richardson submitted with this Response, Applicants' claimed invention is surprisingly simpler and more efficient (e.g., reverse transcription proceeds more efficiently), and requires fewer amplification cycles, than methods of the Richardson *et al.* publication. There is nothing in the art that would lead an ordinarily skilled artisan to predict that Applicants' claimed invention would be more efficient or require fewer amplification cycles.

An invention that provides the discovery and solution to a problem that is not appreciated in the art is further evidence against a *prima facie* case of obviousness. *Eibel Process Co. v. Minnesota and Ontario Paper Company*, 261 US 45 (1923). As noted previously, Applicants' claimed invention solves problems that are not even addressed or recognized in the cited publications. For example, as Dr. Richardson indicates in the attached Declaration, by comparison with the procedure in the Richardson *et al.* publication, the present invention advantageously avoids the need for rare restriction sites, and it allows for the inclusion of specific restriction sites for lambda cloning.

Another advantage of the claimed method as explained by Dr. Richardson in his Declaration is that the production of complex products is minimized, due in part to the use of unique sequences in the heeled 5'-amplification primer (FAP) and the heeled 3'-amplification primer (TAP) which are absent from the genome being investigated. Moreover, while the procedure described in the Richardson *et al.* publication uses a single primer to amplify the products after reverse transcriptase and second strand synthesis, Dr. Richardson explains that the present invention provides the significant advantage that two separate primers of unique sequence are used (see point 5 of Dr. Richardson's Declaration). In addition, Applicants' claimed invention not only provides greater amplification but also greater flexibility in use. For example, it readily allows the inclusion of specific restriction sites, for manufacturing subtracted normalized and enriched cDNA libraries, for fragmentation, and for use as probes on the microarrays and filters. As can be understood from the above, and from Dr. Richardson's Declaration, there are several surprising advantages of Applicants' claimed invention over the teachings of the cited references. Dr. Richardson concludes in his Declaration that, at the time of the present invention, he would not have expected that combining reverse transcription and amplification steps would have resulted in the many advantages described above. Thus, Applicants maintain that their claimed invention is not obvious over the cited publications. Accordingly, reconsideration and withdrawal of the rejections under 35 USC §103 is respectfully requested.

In view of the foregoing remarks, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachment: Declaration of Dr. Peter Richardson under 37 CFR §1.132